

DATA EVALUATION RECORD

1. CHEMICAL: Actellic 5 E
2. TEST MATERIAL: Pirimiphos Methyl Technical (89.9%), a pale brown liquid.
3. STUDY/ACTION TYPE: Avian Acute Oral LD50
4. STUDY IDENTIFICATION: Ross, D. B., N. L. Roberts, and C. Fairley, 1979. The Acute Oral Toxicity (LD50) of Pirimiphos Methyl to the Mallard Duck. Conducted at Imperial Chemical Industries Ltd., Huntington Research Centre, Huntington, England. EPA accession No. 413110-01. Submitted by ICI Americas Inc., Wilmington, Delaware. Accession #413110-01.
5. REVIEWED BY:
Mark R. Roberts
Wildlife Biologist
Ecological Effects Branch
Signature: *Mark R. Roberts*
Date: 1/16/90
INVALID
6. APPROVED BY:
Ann Stavola
Acting Head, Section III
Ecological Effects Branch
Signature: *M. Repcode for Stavola*
Date: 2/16/90
7. CONCLUSIONS: This study is not scientifically sound, and does not fulfill guideline requirements for an avian single-dose oral LD50 test. Without the data and information that is needed to validate this study (See Items 14A,C,D) the reliability of the reported LD50 is questioned.
8. RECOMMENDATIONS: N/A



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9. BACKGROUND:

10. DISCUSSION OF INDIVIDUAL STUDIES OR TESTS: N/A

11. METHODS AND MATERIALS:

Species. Anas platyrhynchos

Age. Only described as "young".

Source and rearing history. Birds were purchased from Lincolnshire Pheasantries Ltd., but information on breeding and rearing history was not reported.

Assignment to treatment groups. Not reported

Acclimation. Birds were maintained under test conditions for 14-15 days prior to testing.

Housing conditions. Birds were housed in floor pens measuring 2 X 1.5 m with wire mesh floors. It was not reported if they were housed individually or communally.

Temperature: 21°C

Humidity: Relative humidity 63%.

Lighting: A controlled lighting pattern was followed.

Fasting. Birds were not fed overnight prior to dosing.

Vehicle. Corn oil was used as a vehicle although the total percentage was not reported.

Controls. Control birds were dosed with corn oil only.

Number of birds/concentration. 10 (5 male, 5 female). Nominal concentrations tested were 0, 96, 172, 309, 556, 1000, 1800, and 3240 mg/kg.

Test design. A range finding test indicated that a satisfactory spread of mortalities could be obtained using the test compound at a concentration of 10% w/v in corn oil. However, this was not the case, and 2 more groups of birds were dosed at a later date with a 30% w/v concentration in corn oil.

Dosing method. The compound was administered by oral gavage, one operator holding open the beak and the other administering the test material using a Ch 14 Nelaton rubber catheter and disposable syringe.

Food consumption. Food (HRC poultry diet) and water were offered ad libitum with the exception of the overnight fast prior to dosing. Food consumption was averaged as g/bird/day over a 6-7 day period based on the treatment group. The control and treatment levels 96, 172, 309, 556, and 1000 were averaged from days -7 to -1, -1 to 7, and 8 to 14. Treatment levels 1800 and 3240 were averaged from days -7 to 0, 0 to 7, and 8 to 14.

Bodyweight measurements. Birds were weighed on days -15, -1, 3, 7, and 14 for the control and first 5 treatment levels; treatment levels 1800 and 3240 were weighed on days -14, -7, 0, 3, 7, and 14.

Observation period. All birds were observed for 14 days post-dosing for signs of toxic effects and mortality.

Necropsies. All birds that died and surviving birds from the 4 highest treatment groups were examined post-mortem.

Statistical analysis. The acute oral LD50 was calculated by the Litchfield and Wilcoxon method.

12. REPORTED RESULTS: The calculated LD50 value was 1695 mg/kg with 95% confidence limits 689-4171 mg/kg. Mortalities per treatment group were as follows:

<u>TREATMENT (ppm)</u>	<u>No. of birds</u>	<u>Mortality</u>
0	10	0
96	10	1
172	10	1
309	10	2
556	10	2
1000	10	4
1800	10	6
3240	10	6

Bird health. Immediately after dosing, all birds showed loss of balance. Recovery of surviving birds was completed between 4 and 7 days and surviving birds appeared in good health for the remainder of the observation period.

Bodyweight. All birds dosed with pirimiphos methyl lost weight between dosing and day 3 of the observation period. With the exception of the 3240 ppm treatment group, all groups increased in weight between days 3 to 7. Bodyweight changes over the 7 to 14 day period were considered to be within normal limits. (See table 2, attached).

Food consumption. Direct comparison between groups was difficult because of spillage, but the results indicate that there was a reduction in food consumption between dosing and day 7 in the treatment groups. The results for the second half of the observation period were considered within normal limits (See table 3, attached).

Necropsies. Only birds with remarkable lesions were reported. (See attachment, below table 3).

13. STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:

"The LD50 value for pirimiphos methyl to the Mallard duck was calculated to be 1695 mg/kg (95% confidence limits 689-4171 mg/kg)."

A GLP statement page stating "This document is not subject to the requirements of 40 CFR Part 160" was included and signed by the sponsor company agent. A statement explaining "that this report provides a correct and faithful record of the results obtained" was included and signed by the conducting laboratory supervisors.

14. REVIEWER'S DISCUSSION AND INTERPRETATION OF THE STUDY:

A. Test Procedure.

Because this study was conducted according to 1978 guidelines, several deviations from the current guidelines (SEP) were noted:

- o There was no breeding history or rearing background information regarding the mallard stock as required by the SEP.

- o The age of the birds was not reported.

- o The SEP recommends that test material be administered without a vehicle if possible. No explanation regarding the use of corn oil was given.

- o The percent by weight of the vehicle was not reported, and 2 test concentrations were used (10% w/v corn oil, 30% w/v in corn oil). The SEP states that the maximum vehicle amount per dose should not exceed 0.1 to 1.0% of body weight, and should be used on a constant volume/body weight basis. Furthermore, it was not clear how the dose preparations were derived.

- o The method used to assign birds to treatment groups was not reported.

o A detailed description of the lighting pattern was not reported. This must be reported as too much light may induce reproduction and impede test results.

B. Statistical Analysis.

The reviewer adjusted the treatment levels to reflect the concentration based upon 100% ai. The LD50 value was then recalculated using EPA's TOXANAL computer program (Stephan's Probit Analysis) (attached).

C. Results/Discussion.

An LD50 value of 1516 mg/kg (95% confidence limits 795-6812 mg/kg; slope = 1.19) would classify Pirimiphos Methyl as slightly toxic to the mallard. The NOEL was < 96 mg/kg based upon loss of balance, food consumption reduction, and loss of bodyweight at the lowest concentration tested.

Since this LD50 estimate is more than 7 times greater than the lowest accepted LC50 value (207 ppm), there are concerns regarding the amount of corn oil used as a vehicle, and the exact methods of determining dosages.

D. Adequacy of the Study.

1. Category: Invalid

2. Rationale: No explanation regarding the use or the amount of the corn oil vehicle was given. The test compound was administered at 2 different base concentrations and the exact amounts test substance, active ingredient, solvent, and carrier were not reported. Why the laboratory practice methods did not conform to 40 CFR Part 160 was not ascertained.

3. Repairability: Yes, can be upgraded to core if the concerns listed in 14A, and those directly above, are adequately addressed.

15. COMPLETION OF ONE-LINER Yes, 01-17-90.

TABLE 2

Group mean bodyweights and bodyweight changes (g/bird)

Group	No. of birds	Dose level (mg/kg)	Sex	Days of study									
				-15	-1	3	7	14	-15 to -1	-1 to 3	3 to 7	7 to 14	
1	5	0	♂	1075	1090	1094	1100	1099	+15	+4	+6	-1	
	5		♀	1195	1163	1151	1130	1094	-32	-12	-21	-36	
2	5	96	♂	1099	1112	1103	1154	1188	+13	-9	+51	+34	
	5		♀	1228	1196	997	1110	1174	-32	-199	+113	+64	
3	5	172	♂	1045	1093	1044	1049	1075	+48	-49	+5	+26	
	5		♀	1244	1197	1098	1109	1142	-47	-99	+11	+33	
4	5	309	♂	1015	1032	1001	1039	1040	+17	-31	+38	+1	
	5		♀	1158	1167	1125	1165	1202	+9	-42	+40	+37	
5	5	556	♂	1081	1092	1026	1091	1125	+11	-66	+65	+34	
	5		♀	837	837	816	880	883	0	-21	+64	+3	
6	5	1000	♂	1183	1164	1045	1157	1210	-19	-119	+112	+53	
	5		♀	1103	1079	918	1012	1120	-24	-161	+94	+108	
				Days of study									
				-14	-7	0	3	7	14	-14 to 0	0 to 3	3 to 7	7 to 14
7	5	1800	♂	1123	1079	1034	865*	945*	1035*	-89	-169	+80	+90
			♀	1050	1031	987	887	968	963	-63	-100	+81	-5
8	5	3240	♂	1142	1107	1070	973	958	1082	-72	-97	-15	+124
	5		♀	1049	1008	996	890*	850*	955*	-53	-106	-40	+105

* One bird only.

During the first 3 days after dosing with pirimiphos methyl there was evidence of a decrease in bodyweight in all test groups. This was followed by a bodyweight increase over the following 4 days in all test groups of birds except those in Group 8 (3240mg/kg) which showed a further decrease in bodyweight. Over the 7 to 14 day period all bodyweight changes were considered to be within normal limits.

FOOD CONSUMPTION

Results are given below in Table 3.

TABLE 3
Group mean food consumption (g/bird/day)

Group	No. of birds	Dose level (mg/kg)	Days of study		
			-7 to -1	-1 to 7	8 to 14
1	10	0	207	143	113
2	10	96	188	115	165
3	10	172	152	103	154
4	10	309	150	109	163
5	10	556	112	102	164
6	10	1000	134	74	202
			Days of study		
			-7 to 0	0 to 7	8 to 14
7	10	1800	77	43	111
8	10	3240	74	18	150

The Mallard duck is a very untidy feeder and the resulting spillage makes comparison between groups difficult. The results indicate that there was a reduction in food consumption over the first 7 days of the post-dose observation period in groups dosed with pirimiphos methyl. The results between Days 7 - 14 were considered to be within normal limits.

GROSS POST-MORTEM EXAMINATION

Birds 561♂ and 554♀ (Group 6, 1000mg/kg) had dark green fluid in the intestines.

Birds 739♂ (Group 7, 1800mg/kg) had a pale liver.

Birds 736♀ (Group 7, 1800mg/kg) had a pale liver and blood in the lungs.

No other abnormalities were observed.

M. Roberts ACTELLIC 5 E Anas platyrhynchos 01-17-90

CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
2913	10	6	60.00001	37.69531
1618	10	6	60.00001	37.69531
899	10	4	40	37.69531
500	10	2	20	5.46875
278	10	2	20	5.46875
155	10	1	10	1.074219
86	10	1	10	1.074219

THE BINOMIAL TEST SHOWS THAT 0 AND +INFINITY CAN BE
USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT
CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL
ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LD50 FOR THIS SET OF DATA IS 1206.061

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LD50	95 PERCENT CONFIDENCE LIMITS
3	1.25215	1405.212	0 +INFINITY

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
3	.3390238	1	.9718641

SLOPE = 1.187973
95 PERCENT CONFIDENCE LIMITS = .4962667 AND 1.879678

* LD50 = 1516.421
95 PERCENT CONFIDENCE LIMITS = 795.0086 AND 6812.343

LD10 = 129.3516
95 PERCENT CONFIDENCE LIMITS = 10.97541 AND 287.4037
